Manitoba
Diabetes
Care Recommendations

Manitoba
Building for the Future

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Care Recommendations

Balance is an essential factor in diabetes prevention, education, care, research and support. The front cover graphic design reflects the concept of the ***medicine circle*** *or* ***medicine wheel****, an ancient and powerful symbol of healing and balance. The quadrants of the circle can be interpreted as representing the importance of balance in all aspects of human existence: spiritual, emotional, physical and intellectual.*

2007-01630/

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Manitoba Diabetes Care Recommendations

Background & Introduction

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Background & Introduction

In June 1996, Manitoba's Minister of Health declared diabetes to be a major public health issue and epidemic in Aboriginal people and Seniors (over age 55 years) of all populations. This was based on evidence documented by the Epidemiology and Diabetes & Chronic Diseases Units of Manitoba Health in their ongoing *Diabetes Burden of Illness Study*.

Diabetes: A Manitoba Strategy is Manitoba's response to the epidemic of diabetes and was released in November 1998. A Steering Committee with five Working Groups addressed the continuum of Diabetes Prevention, Education, Care, Research and Support.

A key recommendation from the Care Working Group was:

'Develop **Manitoba Diabetes Care Recommendations** for the care of people with diabetes, consistent with the Canadian Diabetes Association Clinical Practice Guidelines.'

In 1992, the Canadian Diabetes Advisory Board first published *Clinical practice guidelines for treatment of diabetes mellitus*. In 1998, the Canadian Diabetes Association re-wrote the guidelines to reflect evidence-based clinical practice. In 2003, the guidelines were extensively revised and expanded to meet the growing needs of diabetes prevention and care. The *Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada* (Can J Diabetes. 2003;27(Suppl 2): S1-152) were published in December 2003.

The 2006 **Manitoba Diabetes Care Recommendations** incorporate and reflect the expansion and revision of the national guidelines.

The **Manitoba Diabetes Care Recommendations** are an adaptation of the national guidelines, for province-wide use in Manitoba. Additional information has been added to provide practical details in specific areas. The goal of the **Manitoba Diabetes Care Recommendations** is to provide the standards of care for diabetes in the community, in a clear and precise format. Issues beyond the scope of these recommendations should be referred to members of a specialized diabetes health care team.

The **Manitoba Diabetes Care Recommendations** provide the evidence and standards of practice for the Manitoba Regional Diabetes Program and Risk Factor & Complication Assessment training.

The intended audience for the **Manitoba Diabetes Care Recommendations** includes primary care physicians, diabetes educators and other health care professionals and providers.

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Prevention

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Prevention

Definition

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, insulin action or both.

Classification

Type 1 Diabetes

- Pancreatic beta cell destruction that usually leads to absolute insulin deficiency
- Prone to diabetic ketoacidosis
- Auto-immune mediated

Type 2 Diabetes

- Ranges from predominantly insulin resistance with relative insulin deficiency to predominantly insulin secretory defect with insulin resistance
- Generally, not prone to diabetic ketoacidosis

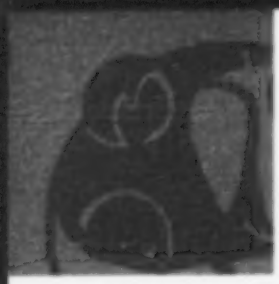
Gestational Diabetes Mellitus

- Glucose intolerance with first onset or recognition during pregnancy

Other

This includes a wide variety of less common conditions, for example:

- genetic defects of pancreatic beta cell function
- genetic defects in insulin action
- drug-induced ex: corticosteroid-induced
- disease of the endocrine pancreas
- endocrine disorders known to cause diabetes.



Diagnosis

DIAGNOSTIC CRITERIA for DIABETES	
In the presence of classical symptoms of diabetes: thirst, frequent urination, blurred vision, fatigue or weight loss	Random Plasma Glucose ≥ 11.1 mmol/L
Fasting Plasma Glucose (FPG)	Fasting Plasma Glucose ≥ 7.0 mmol/L
75 gram Oral Glucose Tolerance Test (OGTT)	2 hour glucose value ≥ 11.1 mmol/L

The FPG of 7.0 mmol/L and 2 hour PG of 11.1 mmol/L represent threshold values for micro and macrovascular complications. The OGTT remains the "gold standard" for the diagnosis of diabetes. However, diabetes is most often diagnosed by use of the first two criteria.

A confirmatory test should be done on a separate day. This second test is not necessary for the diagnosis of diabetes in children or adults with classical symptoms, as metabolic decompensation may occur quickly. Glycated hemoglobin (A1C) is not recommended as a test for diagnosis.

PLASMA GLUCOSE VALUES for DIAGNOSIS of IFG, IGT and DIABETES			
	FPG (mmol/L)		2hPG in a 75-g OGTT (mmol/L)
IFG	6.1-6.9		NA
IFG (isolated)	6.1-6.9	and	< 7.8
IGT (isolated)	< 6.1	and	7.8-11.0
IFG and IGT	6.1-6.9	and	7.8-11.0
Diabetes	≥ 7.0	or	≥ 11.1

Used with permission from Can J Diabetes. 2003;27(suppl 2):51-5152

2hPG = 2-hour plasma glucose
FPG = fasting plasma glucose
IFG = impaired fasting glucose
IGT = impaired glucose tolerance
NA = not applicable
OGTT = oral glucose tolerance test
PG = plasma glucose

Prediabetes

Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) identify earlier stages of glucose intolerance or prediabetes. Prediabetes is a practical term that refers to either IFG or IGT. Both are associated with an increased risk of developing type 2 diabetes. IGT alone is also associated with an increased risk of developing cardiovascular disease (CVD).

Screening for Type 2 Diabetes

Whole population screening for type 2 diabetes is not recommended. Regular testing for type 2 diabetes should be part of a person's periodic health assessment performed by a primary health care provider.

Guidelines for Screening

Testing for type 2 diabetes in individuals without risk factors is recommended every 3 years, beginning at age 40. Individuals with risk factors should be tested more frequently and/or from an ealier age.

Risk Factors for Type 2 Diabetes

- First degree relative with type 2 diabetes
- Member of a high-risk group (for example, Aboriginal, Hispanic, Asian, South Asian or African descent)
- History of IGT or IFG
- History of gestational diabetes
- Hypertension
- Dyslipidemia
- Overweight or obesity, particularly abdominal obesity
- Vascular disease
- Presence of diabetes-related complications
- Polycystic ovarian syndrome (PCOS)
- Acanthosis nigricans
- Schizophrenia and/or use of atypical antipsychotic medications

The recommended test is a Fasting Plasma Glucose (FPG), using a fasting venous sample.

Capillary screening with a glucose meter is acceptable when:

- trained individuals are performing the test and appropriate follow-up testing is arranged, and
- a quality assurance program is in place to monitor the accuracy of results.

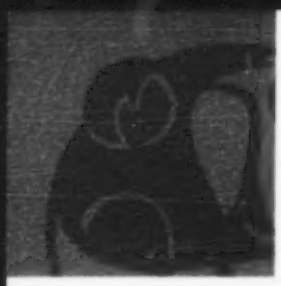
Screening for Type 2 Diabetes in Children

Obese children ≥ 7 years of age should be considered for screening for type 2 diabetes every 2 years using a FPG test, if they meet 2 of the following criteria:

- member of a high-risk ethnic group
- family history of type 2 diabetes, especially if the child was exposed to diabetes in utero
- acanthosis nigricans
- PCOS
- hypertension
- dyslipidemia.

A Fasting Plasma or Fasting Capillary Glucose ≥ 7.0 mmol/L is positive for diabetes. A confirmatory test should be done on a separate day utilizing a fasting venous sample.

This second test is not necessary for the diagnosis of diabetes in children or adults with classical symptoms, as metabolic decompensation may occur quickly.



Risk Factor Assessment for Type 2 Diabetes and Cardiovascular Disease

The metabolic syndrome of insulin resistance is a common metabolic state characterized by some or all of the following conditions:

- insulin resistance and abnormal glucose tolerance and/or diabetes
- overweight
- abdominal obesity
- hypertension
- dyslipidemia
- vascular disease
- PCOS
- acanthosis nigricans.

Individuals with the metabolic syndrome have a significant risk of developing cardiovascular disease.

Strategies for Prediabetes States

For individuals with prediabetes, the following strategies can be used:

- a structured program of lifestyle modification that includes moderate weight loss and regular physical activity should be implemented to reduce the risk of type 2 diabetes.
- pharmacologic therapy with metformin (biguanide) or acarbose (alpha-glucosidase inhibitor) can be considered in individuals with IGT. Some evidence now suggests that a thiazolidinedione (TZD) could also be considered.

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Education

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Education

Diabetes Health Care Team

Diabetes care requires the daily commitment of the person with diabetes to balance appropriate lifestyle choices and pharmacologic therapy, through the acquisition of specific self-management diabetes knowledge and skills. Initial and ongoing diabetes education for the person with diabetes and his or her family should be considered an integral part of diabetes care. This requires the support of a multidisciplinary team of diabetes health care professionals and providers. The Diabetes Health Care (DHC) team is the structure that provides this support.

Central to the DHC team is the person with diabetes and his or her family. Also central to this team is the primary care physician and/or a diabetes specialist as well as the team of community-based diabetes educators and diabetes health care providers. All children with type 1 diabetes and their families should be referred to a DHC team for children and adolescents immediately upon diagnosis.

When required, the DHC team may be expanded to include other health care and community service specialists and providers. The DHC team should provide comprehensive, shared care that facilitates ongoing participation and communication amongst all its members.

Target Blood Glucose and A1C Levels

TARGET BLOOD GLUCOSE and A1C LEVELS for ADULTS[1]			
	A1C (%)	FPG/preprandial PG (mmol/L)	2-hour postprandial PG (mmol/L)
Target for most patients	**≤ 7.0**	**4.0 – 7.0**	**5.0 – 10.0**
Normal range (consider for patients in whom it can be achieved safely)	≤ 6.0	4.0 – 6.0	5.0 – 8.0

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[1] Treatment goals and strategies must be tailored to the person with diabetes, with consideration given to individual risk factors.

A1C = glycated hemoglobin FPG = fasting plasma glucose PG = plasma glucose

TARGET BLOOD GLUCOSE and A1C LEVELS for CHILDREN and ADOLESCENTS			
Age (years)	**A1C (%)**	**Preprandial PG (mmol/L)**	**Considerations**
<5	≤ 9.0	6-12.0	Extreme caution is required to avoid severe hypoglycemia because of the risk of cognitive impairment in this age group
5-12	≤ 8.0	4.0-10.0	Targets should be graduated to the child's age
13-18	≤ 7.0	4.0-7.0	Appropriate for most patients
	≤ 6.0	4.0-6.0	Consider for patients in whom these targets can be achieved safely

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A1C = glycated hemoglobin PG = plasma glucose

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Clinical Assessment

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Clinical Assessment

History

Current Status

- Time of onset and progression of symptoms of diabetes (thirst, urinary frequency, blurred vision, weight loss, infections of the urinary tract, skin or vaginal areas)
- Presence of symptoms of diabetes-related complications including eye, kidney, cardiovascular, cerebrovascular and peripheral vascular function, neurological function, hypoglycemia unawareness, skin and foot problems

Diabetes Assessment

- Previous diabetes education
- Self Blood Glucose Monitoring (SBGM)
  - Current records
  - Frequency
  - Lab/meter correlation
- Eating habits including meal/snack frequency and composition, food choices and weight history
- Level of physical activity
- Diabetes medications
  - Oral agents
  - Insulin dosage, adjustment and algorithms
- Hypoglycemia - frequency and awareness
- Vaccination status in adults - influenza and pneumococcus
- Health determinants including family and/or other supports, education, employment and health beliefs

Diabetes Complication Risk Factor Assessment

- Review of previous
  - A1C values
  - BP
  - BMI / waist circumference (WC)
  - Lipid profile
  - Microalbuminuria screen
  - Monofilament assessment of feet
  - Retinopathy screen

Past History

- Gestational diabetes
- PCOS
- Cardiovascular (CVD), cerebrovascular (CVA) and/or peripheral vascular disease (PVD)
- Conditions requiring long-term corticosteroid use (as a cause of diabetes)
- Pancreatic disease (as a cause of diabetes)
- Depression

Family History

- Diabetes
- Cardiovascular disease
- Hypertension
- Dyslipidemia
- Autoimmune disease (type 1 diabetes)

Medications

- All prescription and non-prescription medications
- Alcohol
- Smoking
- Allergies

Physical Exam

General

- BMI: kg/m²
- WC
- Pulse and BP

Head & Neck

- Eyes
  - Cataracts
  - Fundoscopic exam (does not replace retinal assessment through dilated pupils by experienced examiner)
- Teeth and gums
- Thyroid

Cardiovascular & Peripheral Vascular Exam

- Presence of signs of congestive heart failure
- Peripheral pulses, bruits

Skin

- Injection sites
- Signs of dyslipidemias
- Acanthosis nigricans
- Infections (ex: fungal)

Foot Exam

- Screening for vascular integrity
  - Colour
  - Skin and nail condition
  - Peripheral pulses
  - Presence of infection or ulceration
- Screening for peripheral neuropathy
  - Semmes-Weinstein 10 gram monofilament assessment
  - Presence of vibration or proprioception senses
  - Presence of ankle reflexes

Investigations

Glycemic Control

- A1C

Complication Risk Factor Assessment

- Baseline serum electrolytes, creatinine and liver function tests in adults
- Fasting lipid profile in adults >30 years
- TSH
- Microalbuminuria screen
- Calculation of creatinine clearance
- Retinal exam through dilated pupils by experienced examiner
- Resting electrocardiogram (EKG) or exercise EKG (if indicated) for adults

CLINICAL DIABETES ASSESSMENT FLOW CHART

	Initial Assessment	Routine Follow-up (2-4 months)	Annually
Clinical Assessment	• Complete history & physical exam including diabetes assessment	Diabetes assessment including: • Review of cardiovascular risk factors • Medication review • BMI / WC • BP • Foot exam as indicated • Neurological assessment as indicated	Update diabetes assessment including: • Review of cardiovascular risk factors • Medication review • BMI / WC • BP • Foot exam • Neurological assessment as indicated • Vaccination status in adults as indicated
Investigations for Glycemic Control	• A1C	• SBGM records • A1C	• Lab/meter correlation
Investigations for Complication Risk Factor Assessment	• Baseline serum electrolytes, creatinine, liver function tests in adults • Fasting lipid profile • TSH • Microalbuminuria screen • Retinal exam • Resting (or exercise) EKG (if indicated) for adults (>30 yrs)	Monitor: • Serum electrolytes, creatinine, liver function tests as indicated • Fasting lipid profile as indicated • Microalbuminuria as indicated	• Retinal assessment through dilated pupils as indicated • Microalbuminuria screen (in the absence of nephropathy) • Determination of creatinine clearance (in the presence of nephropathy)
Diabetes Care Plan	• Determination of target blood glucose goals • Diabetes Education • Glycemic control/ complication monitoring and interventions	• Progress towards target blood glucose goals • Diabetes Education • Glycemic control/ complication monitoring and interventions	• Progress towards target blood glucose goals • Diabetes Education • Glycemic control/ complication monitoring and interventions

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b Oral Antihyperglycemic Agents

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Oral Antihyperglycemic Agents

Guidelines For Use

Oral antihyperglycemic agents (oral agents) are one component of management for type 2 diabetes. The diabetes care plan must begin with and continually emphasize the key principles of healthy eating and increased physical activity.

There is a need for aggressive action and timely reassessment in attaining blood glucose targets as it is now understood that short-term hyperglycemia can result in complications.

The choice of oral agent(s) is individually determined. Combinations of oral agents in submaximal dosages may produce more rapid and improved glycemic control. Oral agents may be used in combination with insulin, particularly intermediate or long-acting insulin once or twice daily.

Contraindications

- Type 1 diabetes.
- Metformin for those individuals with renal impairment (creatinine clearance <60 mL/min or serum creatinine >130 µmol/L), hepatic impairment (AST/ALT > 3x upper limit of normal) or significant congestive heart failure.
- Thiazolidinediones (TZDs) should not be used in combination with daytime insulin.
- Women of childbearing age (oral agents are possibly teratogenic).
- Children <18 years with type 2 diabetes is a relative contraindication, as few studies indicating safety or efficacy have been reported in this age group. In adolescents with type 2 diabetes, metformin or insulin may be considered if glycemic targets are not met through lifestyle changes.

Oral Agents and Seniors

Risk of hypoglycemia and drug interactions must be considered. Gliclazide or glimepiride may be preferable to glyburide as they are associated with less risk of hypoglycemia. Glyburide often is the cause of significant hypoglycemia.

Start with a low dose and increase slowly. Side effects of medications may be much more debilitating in an older person.

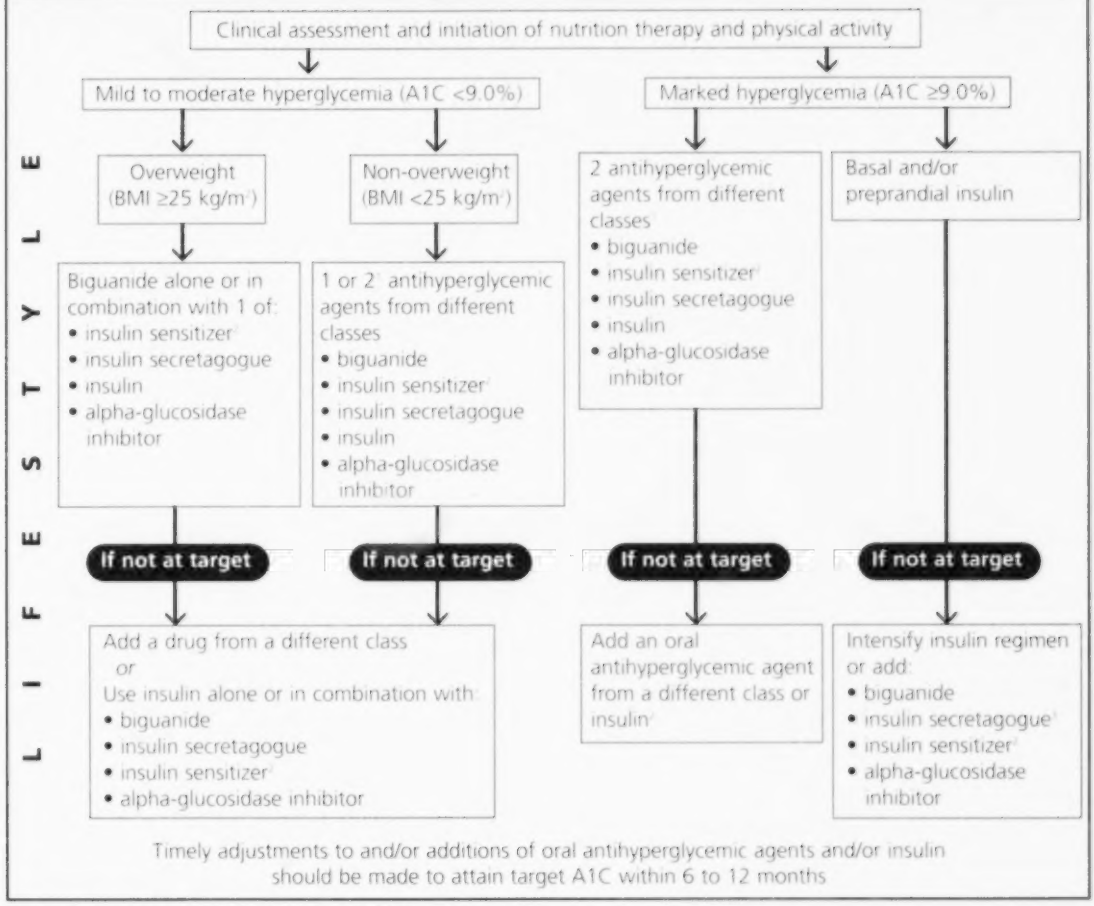
ORAL ANTIHYPERGLYCEMIC AGENTS

Oral Agent	Mechanism of Action	Dosage	Action Time	Benefits	Disadvantages
Biguanides (Insulin Sensitizer)					
Metformin Glucophage	• Insulin sensitizer • Reduces hepatic glucose output	• Start 250-500 mg bid ac meals • Start with low dose and increase slowly • Maximum dose 2550 mg/day in divided doses	8 hrs	• Does not promote weight gain • Rarely causes hypoglycemia • Can be used in combination with daytime insulin	GI: • nausea • bloating • diarrhea Slow increase in dose decreases these side effects **Contraindicated with renal or hepatic impairment, or CHF**
Sulfonylureas (Insulin Secretagogue)					
Glyburide Diabeta	Stimulates pancreatic secretion of insulin	• Start 2.5-5 mg od or bid ac meals • Maximum dose 10 mg bid	16-24 hrs		• May cause weight gain • May cause hypoglycemia
Gliclazide Diamicron	as above	• Start 80 mg od • Maximum dose 160 mg bid	8-16 hrs	Causes less hypoglycemia than glyburide	• May cause weight gain
Diamicron MR	as above	• Start 30 mg od • Maximum dose 120 mg od	24 hrs		
Glimepiride Amaryl	as above	• Start 1-2 mg od • Dosage range is 1-8 mg od	24 hrs	• May be used in combination with daytime insulin • May cause less hypoglycemia than glyburide	• May cause less weight gain

ORAL ANTIHYPERGLYCEMIC AGENTS

Oral Agent	Mechanism of Action	Dosage	Action Time	Benefits	Disadvantages
Alpha-Glucosidase Inhibitors					
Acarbose Prandase	• Inhibits glucosidase enzymes in carbohydrate digestion • Decreases post-prandial glucose rise	• Start 25 mg with first bite of food • Titrate weekly to usual dose of 50-100 mg/meal	Best effect seen post-prandially	No hypoglycemia if used alone	• GI: bloating, flatus • Start with low dose and increase slowly to decrease GI side effects • "Beano" counteracts action • When treating hypoglycemia in the presence of acarbose, use dextrose tablets, milk or honey
Meglitinides (Insulin Secretagogue)					
Repaglinide Gluconorm	• Stimulates pancreatic insulin secretion • Different mechanism from sulfonylureas	• Start 0.5 mg taken 0-30 min before each meal • Or titrate according to CHO intake (1 mg/15g CHO) • Dosages available as 0.5,1, 2 mg	Short-acting; stimulates insulin secretion in response to glucose rise at meal time	• Controls post-prandial glucose rise • Provides flexibility to fit varied meal-times	• May cause hypoglycemia
Thiazolidinediones or TZDs (Insulin Sensitizer)					
Rosiglitazone Avandia	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	2-8 mg daily as a bid dosage	Effect seen after 6 weeks		• May cause weight gain, peripheral edema, macular edema or rarely CHF • Contraindicated in CHF, hepatic impairment (monitor LFTs regularly) • Should not be used in combination with daytime insulin
Pioglitazone Actos	• Insulin sensitizer • Insulin action improved in liver, muscle and adipose tissue	15-45 mg daily	Effect seen after 6 weeks	May ↓ TG, ↑ HDL	• May cause weight gain, peripheral edema, macular edema or rarely CHF • Contraindicated in CHF, hepatic impairment (monitor LFTs regularly) • Should not be used in combination with daytime insulin
Rosiglitazone/ Metformin Combination Avandamet	As per rosiglitazone and metformin	R(1-4 mg)/ M(500-1000 mg)	As per rosiglitazone and metformin		

MANAGEMENT of HYPERGLYCEMIA in TYPE 2 DIABETES


Clinical assessment and initiation of nutrition therapy and physical activity
Mild to moderate hyperglycemia (A1C <9.0%)
Marked hyperglycemia (A1C ≥9.0%)
LIFESTYLE
Overweight (BMI ≥25 kg/m²)
Non-overweight (BMI <25 kg/m²)
2 antihyperglycemic agents from different classes
• biguanide
• insulin sensitizer[2]
• insulin secretagogue
• insulin
• alpha-glucosidase inhibitor
Basal and/or preprandial insulin
Biguanide alone or in combination with 1 of:
• insulin sensitizer[2]
• insulin secretagogue
• insulin
• alpha-glucosidase inhibitor
1 or 2[3] antihyperglycemic agents from different classes
• biguanide
• insulin sensitizer[2]
• insulin secretagogue
• insulin
• alpha-glucosidase inhibitor
If not at target
If not at target
If not at target
If not at target
Add a drug from a different class
or
Use insulin alone or in combination with:
• biguanide
• insulin secretagogue
• insulin sensitizer[2]
• alpha-glucosidase inhibitor
Add an oral antihyperglycemic agent from a different class or insulin[2]
Intensify insulin regimen or add:
• biguanide
• insulin secretagogue[3]
• insulin sensitizer[2]
• alpha-glucosidase inhibitor
Timely adjustments to and/or additions of oral antihyperglycemic agents and/or insulin should be made to attain target A1C within 6 to 12 months

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[1] May be given as a combined formulation: rosiglitazone and metformin (Avandamet).
[2] When used in combination with insulin, insulin sensitizers may increase the risk of edema or CHF. The combination of an insulin sensitizer and insulin is currently not an approved indication in Canada.
[3] If using preprandial insulin do not add an insulin secretagogue.

A1C = glycosylated hemoglobin BMI = body mass index CHF = congestive heart failure

THERAPEUTIC NOTES

Key adverse effects

Gastrointestinal upset, loose bowels
biguanide, alpha-glucosidase inhibitor

Hypoglycemia
insulin, insulin secretagogues (less with gliclazide, glimepiride and repaglinide than with glyburide)

Edema, fluid retention
insulin sensitizers, rarely with insulin

Moderate weight gain
insulin, insulin secretagogues, insulin sensitizers

Key precaution/contraindications

Hepatic disease
glyburide, biguanide, insulin sensitizers

Significant renal insufficiency
biguanide, sulfonylureas

Significant cardiac failure
biguanide, insulin sensitizers

Sulfa allergy
sulfonylureas

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Insulin C

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Insulin

Guidelines For Use

Type 1 Diabetes

Insulin is essential for people with type 1 diabetes and should be initiated at the time of diagnosis. Referral to a specialized DHC team is recommended for children and adolescents immediately upon diagnosis.

A basal/bolus regimen with the support of a DHC team is strongly recommended for individuals with type 1 diabetes. Basal/bolus regimens use intermediate-acting (NPH) insulin or a long-acting insulin analogue (glargine or detemir) once or twice daily as the basal insulin and a rapid-acting (lispro or insulin aspart) as the bolus insulin for meals.

Type 2 Diabetes

Insulin may be very effective in improving glycemic control in people with type 2 diabetes who have not achieved target blood glucose levels through lifestyle changes and/or oral antihyperglycemic agents. Insulin may be the appropriate first choice treatment in individuals with consistent hyperglycemia (PG > 15 mmol/L).

A basal/bolus regimen is recommended for young adults with type 2 diabetes who require insulin and can be considered for any person with type 2 diabetes.

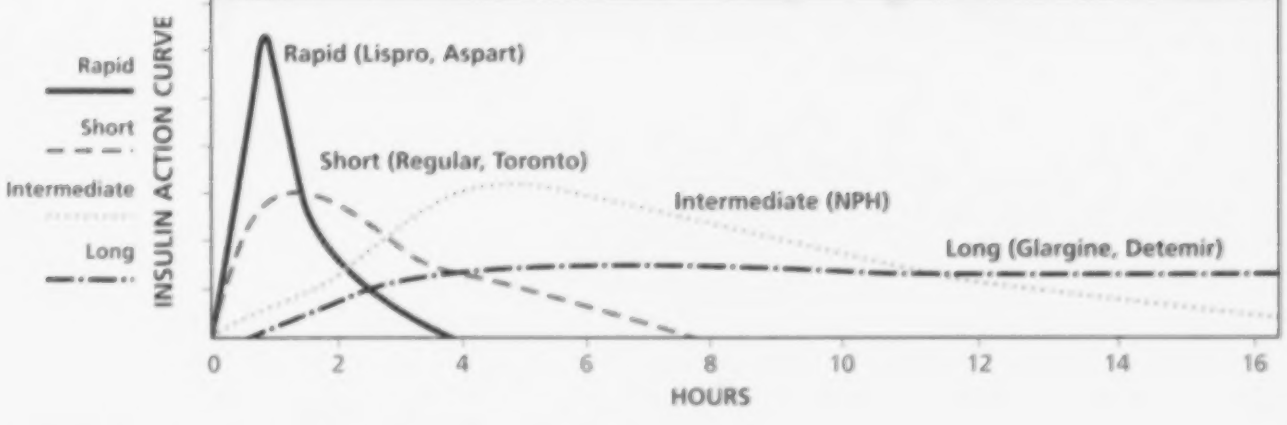
Insulin Initiation - General Notes

- Insulin can be started on an outpatient basis.
- Diabetes education and support is necessary. Close contact between the DHC team and the person starting insulin is needed to review the impact of food intake (including carbohydrate counting), activity, insulin injection technique, SBGM interpretation, dosage adjustments and problem solving.
- Several regimens are possible. All regimens need to be individualized to the person with diabetes.
- A basal/bolus or multiple dose insulin regimen using intermediate or long-acting insulin for the basal dose and rapid-acting insulin for the bolus dose is increasingly preferred. Support from a DHC team will be required.
- Insulin pump therapy (continuous subcutaneous insulin infusion or CSII) should be initiated by a DHC team involving a diabetes specialist.

INSULIN TYPES

Type	Trade Name	Onset	Peak	Duration
Rapid Acting Insulin Analogue				
LISPRO (H)	Humalog	10-15 min	1.0-1.5 hrs	3-5 hrs
ASPART (NR)	NovoRapid	10-15 min	1.0-1.5 hrs	3-5 hrs
Short Acting				
REGULAR (R)	Humulin R Novolin ge Toronto	0.5-1 hr	2-4 hrs	6-8 hrs
Intermediate Acting				
NPH (N)	Humulin N Novolin ge NPH	1-3 hrs	4-8 hrs	12-18 hrs
Long Acting Insulin Analogue				
Glargine (La) Detemir (D)	Lantus Levemir	90 min	No peak	24 hrs
Premixed (Short/Intermediate Acting, R/NPH)				
10/90 30/70* 40/60 50/50	Humulin (*premix available) Novolin ge	0.5 hr	2-12 hrs 2-3 hrs 1 hr	12-18 hrs 12-18 hrs 12-18 hrs
Premixed Insulin Analogue				
25% Rapid Acting and 75% Intermediate Acting	Mix 25	15 min (Rapid Acting portion)	1 hr	10-14 hrs
30% Rapid Acting and 70% Intermediate Acting	NovoMix 30			

INSULIN ACTION

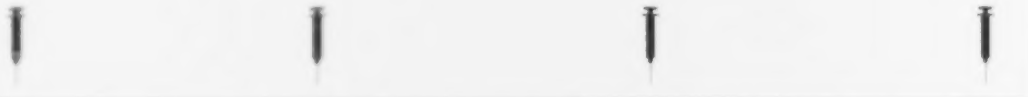


Insulin Regimens

BASAL/BOLUS: QID

Indications: Either type 1 or type 2 diabetes for optimal control. This regimen requires close contact with the DHC team.

Dosage: 40 to 50% of TDD (N,La,D) at hs. Balance given as premeal H,NR based on insulin/CHO ratio.



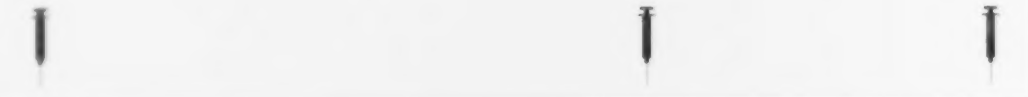
H,NR amac	and	H,NR lunch	and	H,NR pmac	and	N,La,D hs

BASAL/BOLUS: TID

N amac and hs and H, NR (or R) amac and pmac.

Indications: Either type 1 or type 2 diabetes; may provide optimal control.

Dosage: 50 to 70% of TDD (2/3 N and 1/3 H, NR) amac and 15 to 25% of TDD (H, NR) pmac and 15 to 25% of TDD (N) at hs.



N & H,NR amac	and	H,NR pmac	and	N hs

amac = before breakfast
R = Regular insulin
N = NPH insulin
BID = twice daily
TDD = total daily dose

pmac = before supper
H = Lispro insulin
La = Glargine insulin
TID = three times daily

hs = bedtime
NR = insulin Aspart
D = Detemir insulin
QID = four times daily

SPLIT/MIXED DOSE: BID

N and R (or H or NR) twice daily.

Indications: Either type 1 or type 2 diabetes; may provide satisfactory and sometimes optimal control.

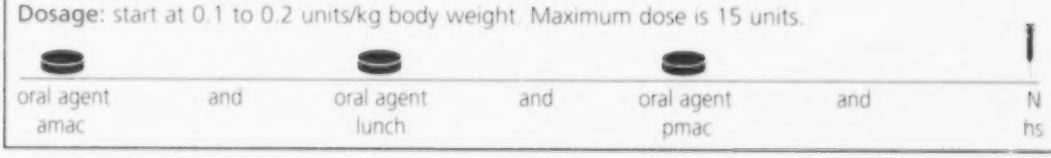
Dosage: 50 to 70% of TDD (2/3 N and 1/3 R) amac and 30 to 50% of TDD (2/3 N and 1/3 R) pmac.

BEDTIME INSULIN AND ORAL AGENTS

N (or La or D) at hs and oral agents during the day.

Indications: Type 2 diabetes, to lower fasting glucose levels and to allow oral agents to have optimal effect.

Dosage: start at 0.1 to 0.2 units/kg body weight. Maximum dose is 15 units.



DAYTIME INSULIN AND ORAL AGENTS

Insulin (single or mixed) twice daily amac and pmac with oral agents (except TZDs).

Indications: Type 2 diabetes.

PREMIX: BID

Indications: Type 2 diabetes, when optimal control is not desired and for those with difficulty mixing insulins. The disadvantage is that specificity in dosage adjustment is lost and a change in dose affects both insulins.

Dosage: 50 to 70% of TDD amac and 30 to 50% of TDD pmac.

amac = before breakfast
R = Regular insulin
N = NPH insulin
BID = twice daily
TDD = total daily dose

pmac = before supper
H = Lispro insulin
La = Glargine insulin
TID = three times daily

hs = bedtime
NR = insulin Aspart
D = Detemir insulin
QID = four times daily

Insulin Therapy for Adults

Basal/Bolus Insulin

This regimen resembles a more physiologic pattern where the basal insulin provides a longer-acting background level of insulin, particularly during the night, and the bolus insulin provides a rapid response to meals. All information regarding bolus insulin refers to the use of rapid-acting insulin, either lispro (Humalog™) or insulin aspart (Novo-Rapid™) only, and cannot be applied to the use of short-acting insulin (Regular™ or Toronto™).

- Basal insulin dosage determined by body size
  - Lean - Start with 5 units of long or intermediate-acting insulin at HS.
  - Non-lean - Start with 10 units of long or intermediate-acting insulin at HS.
  - Titrate the dose by 2 units every 3 days until target blood glucose levels are reached (target FPG and pre-meal PG 4-7 mmol/L).
- Basal insulin dosage determined by body weight
  - The basal dosage is determined by a weight calculation (0.2-0.3 units/kg to start).
- Bolus insulin dosage determined by CHO counting
  - Start with 1 unit rapid-acting insulin per 15 grams CHO. The bolus insulin/CHO ratio will need to be individualized after a trial period.
  - Use a 'correction' algorithm to correct for pre-meal blood glucose levels over target. For every 3 mmol/L blood glucose > 7 mmol/L, add 1 extra unit of rapid-acting insulin to the pre-meal total dose.
  - If vigorous physical activity is planned within 2 hours post meal, decrease the planned bolus insulin dose by approximately 50%.
  - Monitoring the 2 hour pc blood glucose will assess whether the pre-meal bolus dose was appropriate (target 2 hr PG 5-10 mmol/L).

Other Insulin Regimens (TID insulin or split/mixed regimens using Regular/NPH insulin)

- Total daily dose (TDD) of insulin will generally range from 0.5 -1.0 unit/kg in divided doses.
- For NPH-only basal insulin or split/mixed insulin regimens, the general recommendation is to start slowly with the TDD ranging from 0.2-0.3 units/kg. In certain situations, such as adding basal insulin to oral agents or when the concern for hypoglycemia exists, the TDD can be lower (0.1-0.2 units/kg).

- To adjust insulin for these types of regimens:
  - Adjust the basal insulin by 1-2 units every 48 hours and reassess to achieve target blood glucose.
  - Adjust the short-acting insulin by 1-2 units every 24 hours and reassess according to SBGM results.
  - Although the daily insulin regimens using basal and short-acting insulins are generally fixed, daily insulin can be adjusted to balance CHO intake and/or physical activity. Increase short-acting insulin by 1-2 units for every pre-meal blood glucose value >3 mmol/L above target. Generally, individual short-acting insulin dosages can be increased to a maximum of 10% of the TDD at any usual dosage time for SBGM values above target. The same adjustment can be used to decrease insulin dosages as necessary.

Insulin Therapy for Children with Type 1 Diabetes

- All children/adolescents with newly diagnosed type 1 diabetes should be referred to a specialized pediatric DHC team immediately upon diagnosis.
- A basal/bolus regimen is recommended for children and adolescents with type 1 diabetes from the time of diagnosis.
- Insulin dosage adjustments need to be made daily during the first 2 weeks following diagnosis.
- For young children, rapid-acting insulin may be given after the meal, thus allowing the dosage to be adjusted for what the child actually eats.
- Insulin requirements will decrease 1-2 months after diagnosis, when weight is regained, appetite decreases and insulin secretion recovers temporarily (honeymoon phase).
- Insulin doses for basal insulin will increase with age and body size.
- Insulin/CHO ratio for bolus insulin will increase with age and body size.
- Correction dose of rapid-acting insulin will vary with age and body size.

Manitoba
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Recommendations

Complication Risk Factor Assessment and Intervention

4

Manitoba
Diabetes
Care Recommendations

Manitoba Diabetes Care Recommendations

Retinopathy

Manitoba
Diabetes
Care Recommendations

Retinopathy

Guidelines for Screening

- Type 1 diabetes: eyes should be examined at 15 years of age or within 5 years of diagnosis.
- Type 2 diabetes: eyes should be examined at diagnosis (or after puberty).
- Screening for retinopathy should be performed by experienced professionals either in-person or through their interpretation of photographs.
- The follow-up interval for those individuals with no or minimal retinopathy is yearly for type 1 diabetes and every 1-2 years for type 2 diabetes.

SCREENING for RETINOPATHY
When to initiate screening
• 5 years after diagnosis of type 1 diabetes in all individuals ≥15 years of age • In all individuals at diagnosis of type 2 diabetes
Screening methods
• 7 standard field, stereoscopic-colour fundus photography with interpretation by a trained reader (gold standard) • Direct ophthalmoscopy or indirect slit-lamp fundoscopy through dilated pupil • Digital fundus photography
If retinopathy is present
• Diagnose retinopathy severity and establish appropriate monitoring intervals (1 year or less) • Treat sight-threatening retinopathy with laser therapy • Review glycemic, BP and lipid control, and adjust therapy to reach targets as per guidelines • Screen for other diabetes complications
If retinopathy is not present
• Type 1 diabetes: rescreen annually • Type 2 diabetes: rescreen every 1-2 years • Review glycemic, BP and lipid control, and adjust therapy to reach targets as per guidelines • Screen for other diabetes complications

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Manitoba
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Nephropathy & Hypertension

Nephropathy Hypertension

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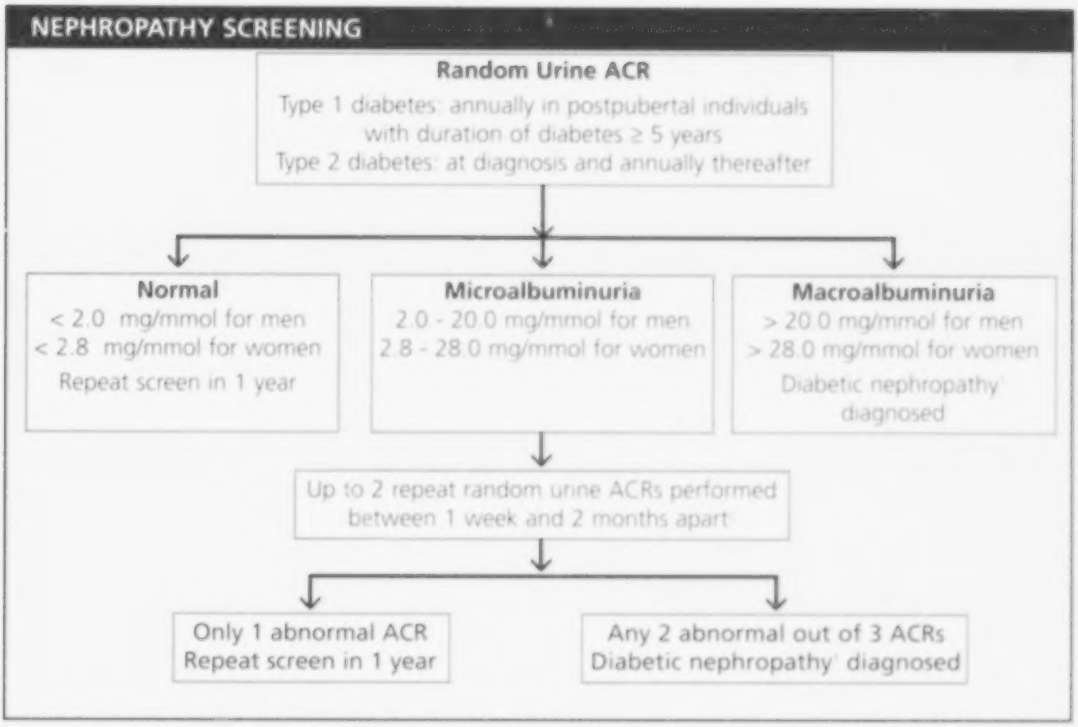
Nephropathy and Hypertension

Frequency

Screening for Nephropathy

- Type 1 diabetes: at 15 years of age or 5 years after the onset of diabetes. Continue screening annually.
- Type 2 diabetes: at the time of diagnosis. Continue screening annually.



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[1] Diabetic nephropathy = microalbuminuria or overt nephropathy (macroalbuminuria)

[2] In adolescents, the preferred confirmation test is a first morning urine sample for ACR or a 12-hour overnight urine collection because of the high frequency of postural albuminuria in normal individuals in this age group.

ACR = albumin to creatinine ratio

FACTORS AFFECTING ACR SCREEN

False Positive

- Exercise within previous 24 hours
- Physiological orthostatic proteinuria
- Short term marked hyperglycemia
- Urinary tract infection
- Uncontrolled hypertension
- Congestive heart failure
- Acute febrile illness

INTERVENTION for MICROALBUMINURIA and/or NEPHROPATHY

1. Management of hypertension **This is the most important aspect of the intervention for microalbuminuria or overt nephropathy.**	• Hypertension in adults with diabetes should be treated to achieve a target BP ≤ 130/80 mm Hg
2. ACE inhibitors or ARB for kidney protective effect	• For adults with type 1 diabetes and microalbuminuria, ACE inhibitors should be used even in the absence of hypertension. An ARB should be substituted for those unable to tolerate an ACE inhibitor. • For adults with type 2 diabetes and a creatinine clearance > 60 ml/min, an ACE inhibitor or ARB should be used. For those with a creatinine clearance ≤ 60 ml/min, an ARB should be used.
3. Optimal glycemic control	• Reinforce physical activity, appropriate food choices, self blood glucose monitoring • Initiate or adjust medication, if necessary
4. Smoking cessation	• Smoking affects renal vasculature and hypertension
5. Assess lipids	• Microalbuminuria can be a marker for dyslipidemia
6. Antiplatelet therapy (ECASA)	• 81-325 mg/day recommended for adults at high CVD risk

ACE = angiotensin converting enzyme
ARB = angiotensin II receptor antagonist

FOLLOW-UP for MICROALBUMINURIA and/or NEPHROPATHY	
1. Treat hypertension	Target BP ≤ 130/80 mm Hg
2. Monitor serum creatinine and creatinine clearance every 6-12 months	Creatinine clearance may be determined using either the Cockcroft-Gault or the MDRD GFR calculator*
3. Monitor ACE/ARB	• Serum creatinine may ↑ to as much as 30% above baseline, stabilizing within 2-4 weeks • No upper limit of creatinine re: contraindication, but caution when creatinine clearance < 30ml/min • Serum potassium • ACR: after 3 months and annually, looking for reduction
4. Indications for referral	• ACR > 75 mg/mmol on more than one occasion • ↑ creatinine > 30% above baseline within 3 months of ACE/ARB • Creatinine clearance < 60 ml/min • Persistent hyperkalemia

*Available at www.nephron.com/cgi-bin/MDRD_GFR.cgi

Hypertension and Diabetes

Hypertension in adults with diabetes (BP > 130/80 mm Hg) should be treated to achieve a target BP ≤ 130/80 mm Hg.

Treatment

- Lifestyle intervention
- Initial antihypertensive treatment (in order of choice)
  Combination treatment often required
  - ACE inhibitor
  - ARB
  - Cardioselective beta blocker
  - Thiazide diuretic
  - Long-acting CCB

ANTIHYPERTENSIVES	
CLASS	**SIDE EFFECTS**
ACE Inhibitor	Hyperkalemia Dry cough Increased serum creatinine
Angiotension II (ARB) Receptor Antagonist	No cough Hyperkalemia Increased serum creatinine
Cardioselective Beta Blocker	May mask symptoms of hypoglycemia, increasing need for SBGM
Thiazide Diuretic low dose (12.5-25 mg)	Increase in blood glucose, usually not significant Hypokalemia
Calcium Channel Blocker (CCB)	Flushing Constipation Peripheral edema

Manitoba Diabetes Care Recommendations

Neuropathy

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Neuropathy

Diabetic neuropathy can affect the sensory, motor or autonomic nervous system.

DIABETIC NEUROPATHY		
CLASSIFICATION	**DESCRIPTION**	**INTERVENTIONS**
Diffuse Symmetrical Polyneuropathy	• Common presentation is peripheral "numbness and tingling" involving hands and feet • Severe presentations have variable types of pain disrupting sleep. Neuropathic pain needs to be distinguished from intermittent claudication	• Amitriptyline • Carbamazepine • Capsaicin topically • Gabapentin **With all therapies, allow 6-8 weeks to see effect.**
Focal Mononeuropathies		
Cranial	• Ex: third nerve palsy with ptosis	• Usually resolves spontaneously
Peripheral	• Ex: carpal tunnel syndrome • Foot drop	• Usually resolves spontaneously
Radiculopathy	• Pain in truncal spinal nerve distribution	• Usually resolves spontaneously
Diabetic Amyotrophy	• Proximal neuropathy manifested by pain, proximal muscle weakness and muscle atrophy	• Usually resolves spontaneously • May respond to treatment for peripheral neuropathy

DIABETIC NEUROPATHY		
CLASSIFICATION	**DESCRIPTION**	**INTERVENTIONS**
Autonomic Neuropathy		
Gastrointestinal dysfunction	• Gastroparesis with vomiting/abdominal bloating and pain	• Gastrointestinal motility drugs: Domperidome Metoclopramide • Frequent small meals • Consider basal/bolus insulin regimen with rapid-acting insulin after meals as blood glucose starts to rise
	• Diarrhea	• Anti-diarrheal medications
	• Constipation	• Increase water and dietary fibre
Genitourinary dysfunction	• Difficulty with micturition • Incontinence or incomplete emptying (neurogenic bladder) • Erectile dysfunction • Retrograde ejaculation	• Options for erectile dysfunction include phosphodiesterase type 5 (PDE5) inhibitors, vacuum pump, intrapenile prostaglandins, injections or prosthesis • Urology referral
Cardiovascular dysfunction	• Postural hypotension • Atypical angina	Postural hypotension • elastic stockings • mineralcorticoid medication Atypical angina • high index of suspicion
Other	• **Hypoglycemia unawareness** (common)	• Frequent SBGM
	• Anhydrosis (lack of sweating, resulting in dry cracked feet in particular)	• Use moisturizers

Manitoba Diabetes Care Recommendations

Foot Complications

Foot Complications

Manitoba
Diabetes
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Foot Complications

Use of Monofilament

The 10 gram Semmes Weinstein Monofilament is a nylon filament mounted on a handle that has been standardized to deliver a 10 gram force when properly applied. Screening with a monofilament is a validated method to assess for peripheral neuropathy and helps determine the risk of foot ulceration. Monofilament screening is part of the complete foot exam as outlined in the Clinical Assessment section.

The monofilament should be applied to the plantar surface of the 5 metatarsal heads and the plantar surface of the great toe. The filament should be applied perpendicular to the skin's surface until it bends slightly (approximately 1 1/2 seconds duration). Avoid ulcer sites, calluses, scars or necrotic tissue. If 3 out of 6 sites are felt, the person is said to have protective sensation. The loss of protective sensation places the person at high risk for foot ulcers.

RISK CATEGORIES and INTERVENTIONS using the SEMMES WEINSTEIN MONOFILAMENT

RISK CATEGORY	CLASSIFICATION	INTERVENTIONS
0	• Intact protective sensation	• Low to no risk of foot complications • Education to be provided • Specialized footwear not necessary at this time • Examine feet at each visit or at least every 4-6 months
1	• Absent protective sensation • Normal foot morphology • No history of ulceration	• Examine feet at each visit or at least four times per year • Appropriately fitted footwear with a soft insole • Education to be provided
2	• Absent protective sensation • Foot deformity present • Plantar ulceration absent	• Examine feet at each visit or at least four times per year • Appropriately fitted footwear with a suitable insole • Education to be provided
3	• Absent protective sensation • History of plantar ulcer	• Examine feet at each visit or at least four times per year • Appropriately fitted footwear with a suitable insole (may need custom footwear) • Education to be provided

CLASSIFICATION and INTERVENTION for DIABETIC FOOT ULCERS		
WAGNER'S GRADE	**CRITERIA**	**INTERVENTIONS**
Grade 0	• Skin intact • No open lesions • May be non-blanching erythema	• Pare callous. Appropriate footwear to protect feet and reduce pressure over pressure points.
Grade 1	• Superficial skin ulceration (may be seen under area of high pressure)	• Pare callous to expose ulcer base. Culture. Saline foot soaks for 10 minutes. • A hydroactive gel (Duoderm™, Intrasite™ or Tegagel™) covered by clean gauze is simplest approach. • Saline wet to dry dressings are an alternative. • May need "wet to dry dressings" using 1/4 strength Eusol™ (sodium hydrochlorite) bid but once wound is clean and provided that granulation tissue is present, hydroactive gel should be substituted for the Eusol. • Protect wound edges with Vaseline, when using Eusol. • Pressure relief is critical for healing and can be accomplished with appropriate footwear, crutches, wheelchairs and casting. • Infected ulcers need antibiotics.
Grade 2	• Deeper ulceration, associated with infection/cellulitis • Does not extend to bone	• X-ray to determine if bone is involved. • Manage the same as Grade 1 ulcer. Use antibiotics.
Grade 3	• Ulcer has extended to deeper tissue layers such as bone • Has abscess formation or osteomyelitis	• X-ray to determine if bone is involved. • Surgical debridement of infected bone. • Appropriate antibiotics administered. • Use non invasive assessment of peripheral circulation (ankle brachial index). Vascular surgical referral may be indicated.
Grade 4 (gangrene)	• Localized gangrene of toes, forefoot, heel	• Manage as for Grade 3 ulcer. • Urgent non invasive assessment of peripheral circulation. Vascular surgical referral may be indicated.
Grade 5 (gangrene)	• Gangrene of entire foot	• Urgent assessment as for grade 4 lesions. • Vascular surgical referral.

ANTIBIOTIC THERAPY for INFECTED ULCERATIONS	
TYPE OF INFECTION	**MEDICATIONS**
Mild	
• Usually associated with cellulitis surrounding an ulceration. • May have a small amount of purulent material at base of ulcer. Usually aerobic gram positive cocci. • May treat as outpatient.	• Cloxacillin 500 mg orally (po) qid • Cephalexin 500 mg po qid • Tmp/Smx 1 DS po bid (Trimethoprim/Sulfamethoxazole) • Clindamycin 300 mg po qid • Amoxacillin and Clavulinic Acid 500 mg po tid
Moderate	
• Range from plantar abscess to cellulitis with tissue necrosis. • Use antibiotics effective against staphlococci, streptococci, anaerobes and enterobacteriaceae. • If not toxic, treat with local incision, drainage and antibiotics. • If toxic, use parenteral antibiotic therapy until stable, then switch to oral therapy (manage as per severe infection - see below).	• Tmp/Smx 1 DS po bid and Metronidizole 500 mg po tid • Tmp/Smx 1 DS po bid and Clindamycin 300 mg po qid • Ciprofloxacin 500 mg po bid and Clindamycin 300 mg po qid • Ciprofloxacin 750 mg po bid and Clindamycin 300 mg po qid • Amoxacillin-Clavulinic Acid 500 mg po tid
Severe	
• Limb or life-threatening infections requiring immediate hospitalization and parenteral antibiotic therapy. • Early surgical debridement and drainage of abscesses is critical! • If in doubt as to appropriate treatment, consult with Infectious Diseases Specialist. • When using aminoglycosides, monitor renal function and aminoglycosides blood levels.	• Clindamycin 600 mg IV every 8 hours (Q8h) and Gentamicin 80 mg IV Q8h • Cefoxitin 2 gm IV Q8h • Cefazolin 2 gm IV Q8h and Metronidazole 500 mg IV Q8h • Piperacillin and Tazobactam 3.375 gm IV Q6h • Clindamycin 600 mg IV Q8h and Cefotaxime 1 gm IV Q8h • Imipenem/Cilistatin 500 mg IV Q6h • Meropenem 1 gm IV Q8h
Osteomyelitis	
• Can be managed with long term oral antibiotic therapy with agents that are well absorbed from the gastrointestinal tract and have good distribution to bone and tissue.	• Tmp/Smx 1 DS po bid and Metronidazole 500 mg po tid • Tmp/Smx 1 DS po bid and Clindamycin 300 mg po qid • Levofloxacin 500 mg po bid and Metronidazole 500 mg po tid • Ciprofloxacin 500 mg po bid and Clindamycin 300 mg po qid • Ciprofloxacin 750 mg po bid and Clindamycin 300 mg po qid

INTERVENTION for FOOT COMPLICATIONS	
COMPLICATION	**INTERVENTIONS**
• Non blanching erythema over pressure points	• Reduce pressure with appropriate foot wear.
• Calluses and corns	• Reduce pressure. Pare carefully. Use pumice stone. Appropriate footwear.
• Cutaneous fungal infections	• Clotrimazole cream 1% or Tolnaftate cream 1% or powder applied twice daily. May require antibiotics for superimposed bacterial infection.
• Intertrigo	• Keep affected skin areas dry. Use antifungal cream.
• Toenail abnormalities	• May be hypertrophic (thick and horn-like). Cut nails every 3-6 weeks straight across to prevent formation of sharp edges.
• Paronychia (nail bed infections)	• Twice daily saline solution soaks and adequate nail care. Systemic antibiotics may be necessary.
• Cellulitis	• Requires antibiotics. The route of administration (oral vs parenteral) will depend on the severity of the infection.
• Claw Foot	• Need appropriate footwear and orthotic devices.
• Charcot Foot	• For the acute Charcot foot, reduce deformity by removing pressure with immobilizing foot in cast. For an established Charcot foot, appropriate insoles and shoes will be required.
• Ischemia	• A painful, cold and white extremity is a surgical emergency (may indicate acute occlusion)!
• Intermittent Claudication	• Regular foot care and as much walking as possible to build collateral blood flow. Referral to a vascular surgeon.

Manitoba
Care
Recommendations

Dyslipidemia

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Care Recommendations

Dyslipidemia

Diabetes significantly increases the risk associated with the complications of atherosclerotic vascular disease, particularly cardiovascular disease (CVD). The non-pharmacologic approach of modifying dietary fat intake and increasing physical activity is the first and key step in improving lipid levels. ECASA at a dose of 81 - 325 mg/day is recommended for adults at high CVD risk.

Most people with diabetes should be considered at high risk for CVD. Some individuals may NOT be considered at high risk such as those who are younger, have a short duration of diabetes, and who do not have diabetes-related complications and other CVD risk factors.

CVD Risk Factors

Screen adults beginning at age 30 if risk factors are present.

- Metabolic syndrome of insulin resistance
- IGT/Diabetes*
- Hypertension*
- Dyslipidemia*
- Obesity, particularly abdominal obesity*
- Family history of premature CVD in a first degree relative (male ≤ 54 yr, female ≤ 64 yr)
- Smoking
- LVH (left ventricular hypertrophy)

*also characteristics of metabolic syndrome

TARGET LIPID VALUE based on LEVEL of RISK	
RISK LEVEL	**LDL-C (mmol/L)**
High (most patients with diabetes)	**≤ 2.0**

HDL-C = high-density lipoprotein cholesterol LDL-C = low-density lipoprotein cholesterol
TC = total cholesterol

For individuals at high risk who also have established CVD, consider target LDL < 1.8 mmol/L. Once LDL target has been met, consider treatment for other lipid targets.

- TC/HDL ratio <4
- TG <1.5 mmol/L
- Apo B <0.9 g/L

TREATMENT OF DYSLIPIDEMIA

LIPID STATUS	THERAPY*
LDL-C above target	Lifestyle modification + Statin
High risk patients with: LDL-C at target and TG level = 1.5-4.5 mmol/L and HDL-C <1.0 mmol/L	Lifestyle modification + Statin or fibrate
TG level >4.5 mmol/L	Lifestyle modification + Fibrate ± statin

*When monotherapy plus lifestyle modification fail to achieve lipid targets, the addition of a second drug from another class should be considered.

LIPID LOWERING AGENTS

CLASS	ACTION	SIDE EFFECTS
Fibrates	• 20-50% ↓ TG • 15-20% ↓ LDL • 10-20% ↑ HDL	• Gastrointestinal • Rare risk of rhabdomyolysis when combined with statins • Modify dose for patients with reduced creatinine clearance
HMG CoA Reductase Inhibitors (Statins)	• 18-55% ↓ LDL • 5-15% ↑ HDL • 7-30% ↓ TG	• Rare risk of rhabdomyolysis when combined with fibrates • Elevated liver enzymes may be seen, regular monitoring is recommended
Nicotinic Acid (Niacin)	• 5-25% ↓ LDL • 15-35% ↑ HDL • 20-50% ↓ TG	• Gastrointestinal • May raise blood glucose levels • Flushing: 325 mg ASA 1 hr before dose • Extended release formulation available
Bile Acid Sequestrants	• 15-30% ↓ LDL • 3-5% ↑ HDL • TG may ↑	• May raise blood glucose levels • Gastrointestinal • May worsen hyper-triglyceridemia
Cholesterol Absorption Inhibitor (Ezetimibe)	↓ LDL	• Few side effects as not absorbed systemically • Will not cause malabsorption of nutrients • Often used in combination with a statin

HDL-C = high-density lipoprotein cholesterol LDL-C = low-density lipoprotein cholesterol
TG = triglycerides

Manitoba
Care
Recommendations

Pregnancy

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Diabetes
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Pregnancy

Gestational Diabetes

Definition

Gestational diabetes is glucose intolerance with first onset or recognition during pregnancy.

Screening and Diagnosis

All pregnant women should be screened for gestational diabetes at 24-28 weeks gestation.

Risk Factors

- Maternal age ≥ 35 years
- Family history of diabetes
- Identified high-risk ethnic groups including Aboriginal, Hispanic, Asian, South Asian and African
- Pre-pregnancy obesity
- PCOS
- Acanthosis nigricans
- Excess weight gain in current pregnancy
- Previous large infant (4000 g)
- Previous gestational diabetes (GDM)
- Corticosteriod use

If a risk factor is identified **during** the pregnancy, screening should be performed at that time. If the screen is negative but the risk factor(s) persist, screening should be repeated in the remaining trimesters.

The preferred screening test is a 50 gram oral glucose load, given at any time of day, followed by a plasma glucose at 1 hour.

- **If the 1 hour value ≥ 7.8 mmol/L, proceed to the OGTT.**
- **If the 1 hour value ≥10.3 mmol/L, the diagnosis of gestational diabetes can be made.**

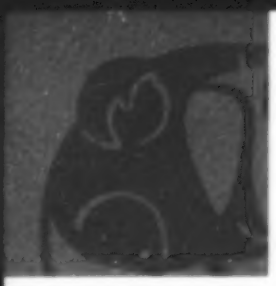
Diagnosis

ORAL GLUCOSE TOLERANCE TEST (2 HOUR 75 GRAM)	
Fasting	≥ 5.3 mmol/L
1 hour	≥ 10.6 mmol/L
2 hour	≥ 8.9 mmol/L

If **2 or more values** are met or exceeded, the diagnosis is **Gestational Diabetes.** If 1 value is met or exceeded, the diagnosis is **Impaired Glucose Tolerance of Pregnancy**.

Impaired Glucose Tolerance of Pregnancy (IGT of Pregnancy) is carbohydrate intolerance in pregnancy and should not be confused with IGT in the non-pregnant person.

IGT of pregnancy carries some of the same implications as does GDM and therefore should be treated in the same fashion.



TARGET BLOOD GLUCOSE LEVELS for PREGNANT WOMEN with GESTATIONAL DIABETES	
Fasting	< 5.3 mmol/L
Post prandial	1 hr < 7.8 mmol/L 2 hr < 6.7 mmol/L

Management

Nutritional therapy is the primary treatment for GDM. Women with GDM should be assessed and followed as required by a registered dietitian (as part of the DHC team) to ensure that the woman's dietary intake/meal plan is appropriate to achieve recommended glycemic control, appropriate weight gain and adequate nutritional intake for both the woman and her baby. Physical activity should be encouraged with individualized frequency, type, duration and intensity.

If the woman with GDM does not achieve glycemic targets within 1-2 weeks of initiating nutritional therapy, insulin should be started. A variety of insulin regimens can be used, including QID, TID basal/bolus and BID split/mixed regimens. Pre-mixed insulins are not recommended. In GDM, strong consideration should be given to using a basal/bolus insulin regimen as this regimen most effectively addresses the post prandial glucose rise typically seen in GDM.

Lispro insulin (Humalog™) can be used in pregnancy. Although placental transport of insulin aspart (Novo Rapid™) has not yet been assessed, it has been shown to be effective in controlling glucose levels in GDM. Rapid-acting insulins are more effective when the dose is adjusted according to a pre-determined insulin/CHO ratio. At this time, glargine and detemir insulin should be avoided and oral hypoglycemic agents (for example, sulfonylureas) are not recommended in pregnancy.

Postpartum Follow-up

Upon delivery, insulin may be discontinued. Postpartum (6 weeks – 6 months), the non-pregnant 75 gram 2 hour OGTT should be performed to assess for the possible development of type 2 diabetes.

Pre-Existing Diabetes and Pregnancy

Ideally, women with pre-existing diabetes will undergo pre-conception planning with their DHC team. Such planning will optimize glycemic control and assess for the presence of any maternal long-term diabetic complications.

Women with either type 1 or type 2 diabetes should optimize glycemic control to attain an A1C ≤ 7.0% in order to decrease the risks of congenital malformations, first trimester spontaneous abortion, pre-eclampsia and progression of retinopathy, particularly for type 1 diabetes.

As part of pre-conception planning:

- Women with type 2 diabetes should discontinue any oral antihyperglycemic agents and begin insulin to attain glycemic targets.
- Women should be screened for microalbuminuria and/or nephropathy. If positive for either, women should attain optimal glycemic and blood pressure control. Those women with nephropathy should be followed carefully as nephropathy may progress during pregnancy.
- Women using ACE inhibitors or ARBs should change to other antihypertensives considered safe in pregnancy.
- Women should undergo a retinal assessment. Repeat retinal assessment should occur as needed during pregnancy and postpartum.
- Women with pre-existing diabetes are at increased risk of having a baby with a neural tube defect. Therefore, it is recommended that all women with pre-existing diabetes take a 5 mg folic acid supplement (available by prescription) from pre-conception through the first 12 weeks of pregnancy.

TARGET BLOOD GLUCOSE LEVELS for PREGNANT WOMEN with PRE-EXISTING TYPE 1 or TYPE 2 DIABETES	
Fasting	< 5.3 mmol/L
Post prandial	1 hr < 7.8 mmol/L 2 hr < 6.7 mmol/L

Management

Similar to insulin use in GDM, a variety of insulin regimens can be used, including QID, TID basal/bolus and BID split/mixed regimens. Pre-mixed insulins are not recommended. As in GDM, strong consideration should be given to using a basal/bolus insulin regimen.

Lispro insulin (Humalog™) can be used in pregnancy. Although placental transport of insulin aspart (Novo Rapid™) has not yet been assessed, it has been shown to be effective in controlling glucose levels in pregnancy. Rapid-acting insulins are more effective when the dose is adjusted according to a pre-determined insulin/CHO ratio. At this time, glargine and detemir insulin should be avoided.

First Trimester

Insulin sensitivity may increase and insulin requirements may actually decrease.

Second and Third Trimesters

Insulin resistance develops, likely through the action of placental hormones and insulin requirements can generally be expected to rise.

Postpartum Follow-up

With delivery, insulin requirements drop significantly. Often, women may require less than their pre-pregnancy insulin dosage for a period of time immediately postpartum.

Acknowledgments

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To ensure consistency with the *Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada*, the Diabetes and Chronic Diseases Unit relied upon the expertise and experience of their medical advisors - Dr. Sora Ludwig, adult medical advisor and Dr. Heather Dean, pediatric medical advisor. Both have full-time academic appointments with the University of Manitoba, in the Section of Endocrinology and Metabolism.

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